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Stop Signal Reaction Time Deficits in a Lifetime Obsessive-Compulsive Disorder Sample

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Abstract

Objectives: Several studies have found impaired response inhibition, measured by a stop-signal task (SST), in individuals who are currently symptomatic for obsessive-compulsive disorder (OCD). The aim of this study was to assess stop-signal reaction time (SSRT) performance in individuals with a lifetime diagnosis of OCD, in comparison to a healthy control group. This is the first study that has examined OCD in participants along a continuum of OCD severity, including approximately half of whom had sub-syndromal symptoms at the time of assessment.

Methods: OCD participants were recruited primarily from within the OCD clinic at a psychiatric hospital, as well as from the community. Healthy controls were recruited from the community. We used the stop signal task to examine the difference between 21 OCD participants (mean age, 42.95 years) and 40 healthy controls (mean age, 35.13 years). We also investigated the relationship between SST and measures of OCD, depression, and anxiety severity.

Results: OCD participants were significantly slower than healthy controls with regard to mean SSRT. Contrary to our prediction, there was no correlation between SSRT and current levels of OCD, anxiety, and depression severity.

Conclusions: Results support prior studies showing impaired response inhibition in OCD, and extend the findings to a sample of patients with lifetime OCD who were not all currently above threshold for diagnosis. These findings indicate that response inhibition deficits may be a biomarker of OCD, regardless of current severity levels.

Keywords

Response inhibition; Anxiety; Biological markers; Cognition; Reaction time; Psychopathology

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INTRODUCTION

Obsessive-compulsive disorder (OCD) is characterized by recurrent, stereotyped, distressing obsessions, and compulsions. It is common in the population and associated with significant impairment and disability (Kessler, Chiu, Demler, Merikangas, & Walters, 2005). OCD is increasingly recognized as arising from dysfunction in frontal-subcortical circuitry. Cognitive studies in OCD most consistently find primary executive functioning deficits, consistent with frontal-subcortical dysfunction (Penades, Catalan, Andres, Salamero, & Gasto, 2005; Rao, Reddy, Kumar, Kandavel, & Chandrashekar, 2008).

Within the past several years, response inhibition has been investigated more frequently in patients with OCD, and several studies have indicated that inhibitory control, or the ability to suppress irrelevant/interfering stimuli or behaviors, is impaired in OCD (Lipszyc & Schachar, 2010; Rao et al., 2008; van Velzen, Vriend, de Wit, & van den Heuvel, 2014). The term “inhibition” refers to a range of cognitive and motor mechanisms. Most commonly, two components of response inhibition are discussed: *restraint*, the ability to withhold a response tendency, and *cancellation*, the ability to stop an action once it has been initiated (Bari & Robbins, 2013; Schachar et al., 2007). The construct of inhibition is particularly relevant to OCD, in that the gold standard therapy for OCD is exposure and response/ritual prevention (ERP), which involves exposure to feared stimuli, with subsequent inhibition of rituals. Although there are no studies directly examining behavioral inhibition in ERP for OCD, one child study has indicated that when therapists and parents discourage avoidance of an exposure stimulus, OCD symptoms reduce in severity (Benito, Conelea, Garcia, & Freeman, 2012). Thus, the inability to inhibit rituals is likely to negatively impact therapy outcomes, and response inhibition likely represents a key mechanism in not just the emergence, but also the persistence of OCD symptoms.

One task that has been shown to be particularly relevant to the measurement of response inhibition in OCD is the stop signal task (SST; Logan, Cowan, & Davis, 1984). This task measures the cancellation of a response, as there is a delay between the “go” cue (stimulus onset) and the onset of the “stop” cue. Multiple studies have demonstrated SSRT impairments in OCD samples (Lipszyc & Schachar, 2010). Studies have indicated that OCD participants (undifferentiated subtypes) have slower SSRT as compared to healthy controls (Boisseau et al., 2012; de Wit et al., 2012; Menzies et al., 2007). OCD participants with contamination and checking symptoms have slower SSRT than controls (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005; Chamberlain et al., 2007). To our knowledge, only one study has indicated no differences between OCD patients and controls in adults (Blom et al., 2011).

Unaffected relatives of OCD patients have also shown slower SSRT as compared to healthy controls, with no difference from OCD participants (Chamberlain et al., 2007; Menzies et al., 2007). However, one study did not find any differences between relatives of OCD patients compared to OCD participants and healthy controls (de Wit et al., 2012). In addition, there is no evidence of a direct relationship between OCD severity and SSRT impairment (Chamberlain et al., 2005, 2007; de Wit et al., 2012). This evidence raises the

possibility that response inhibition deficits may represent an abnormal trait marker in OCD and may not be directly related to severity of behavioral symptoms.

To our knowledge, no one has examined a sample of OCD patients with a lifetime diagnosis of OCD across a range of current symptom severity. We examined stop signal reaction time in participants with OCD as compared to healthy controls across two sequential blocks of the SSRT. We hypothesized that participants with OCD would show slower SSRT as compared to healthy participants. We also correlated SSRT with OCD symptomology to determine if there was a relationship in a sample of participants with more heterogeneous levels of severity.

METHODS

Participants

Twenty-one participants with a lifetime diagnosis of OCD were recruited from our hospital clinic, as well as from the general community. Forty-nine healthy controls were also recruited from the local community through flyers at local shops and universities. Eight of the controls were removed, as they had YBOCS severity scores over 8, and one was removed due to SCID-diagnosed bipolar disorder. Thus, 40 healthy control participants were included in the final sample. See Table 1 for demographic and clinical characteristics.

OCD participants met DSM-IV criteria for a lifetime diagnosis of obsessive-compulsive disorder. Exclusion criteria for the OCD group included current or past psychotic disorder or a clinical history of post-traumatic stress disorder (PTSD). Controls were free of current psychiatric disorders or past anxiety disorder. Ninety percent of OCD participants were receiving medication. Participants within the OCD sample were prescribed SSRIs ($n = 16$), benzodiazepines ($n = 10$), tricyclic antidepressants ($n = 4$), antipsychotics ($n = 2$), and atypical antidepressants (e.g., Wellbutrin, Effexor; $n = 8$). Informed consent was obtained for this Butler Hospital IRB-approved study.

Procedures

Structured Clinical Interview for DSM-IV—The Structured Clinical Interview for DSM-IV (SCID-IV; First, Spitzer, Gibbon, & Williams, 2002) is a semi-structured interview for making major Axis I diagnoses. It is administered by trained evaluators and includes an introductory overview, followed by specific diagnostic modules.

Yale-Brown Obsessive Compulsive Scale—The Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman, Price, Rasmussen, Mazure, Delgado, et al., 1989) is an evaluator-administered questionnaire assessing severity of OCD symptoms, separated by obsessions and compulsions.

Hamilton Depression Rating Scale (HDRS; Hamilton, 1960)—The Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) is an evaluator-administered questionnaire assessing severity of depressive symptoms.

Hamilton Anxiety Rating Scale (HARS; Hamilton, 1959)—The Hamilton Anxiety Rating Scale (HARS; Hamilton, 1959) is an evaluator-administered questionnaire assessing severity of symptoms of anxiety.

Y-BOCS Symptom Checklist (Y-BOCS SC; Goodman, Price, Rasmussen, Mazure, Fleischmann, et al,, 1989)—The Y-BOCS Symptom Checklist (Y-BOCS SC; Goodman, Price, Rasmussen, Mazure, Fleischmann, et al., 1989) is a questionnaire assessing presence of current or past OCD symptoms.

Stop Signal Task—We used a computerized version of the stop-signal task to assess inhibition of prepotent motor responses (Logan et al., 1984). The task, adapted from Aron, Fletcher, Bullmore, Sahakian, and Robbins (2003), was made slightly shorter to reduce participant fatigue. Total task time (after practice trials) was approximately 13 min. Participants underwent practice trials in which they were instructed that speed and accuracy were both important and were trained to inhibit themselves on approximately 50% of the trials. They then watched a computer screen on which a series of two blocks of 128 arrows per block were visually presented. Arrows pointed to either the right (50%) or the left (50%), and subjects responded accordingly by pressing the appropriate button.

The presentation order of right- and left-pointing arrows was randomized. In a randomly assigned proportion (25%) of trials, an audible stop-signal was heard after presentation of the arrow, and subjects were instructed to inhibit their motor response on these trials. On stop trials, the delay between the stimulus onset and the tone is termed the stop-signal delay (SSD). The inter-stimulus interval and the stop-signal delay were varied according to the subject's performance, such that, subjects were able to successfully inhibit their responses on 50% of the stop trials. From these behavioral data, the stop-signal reaction time (i.e., processing time required to inhibit a prepotent motor response) was calculated for each subject. SSRT was estimated by subtracting average SSD from median no-signal reaction time.

Data Analysis

Groups did not differ with regard to education, but the OCD group was significantly older than the healthy control group ($t(59) = -2.12$; $p = .038$); thus, age was included as a covariate in the analyses. Analysis of covariance (ANCOVA) was carried out to examine between-group differences between OCD and healthy controls, controlling for age. *Post hoc* analyses examined differences between the two groups on block 1 and block 2 of the SST. A partial correlation with Pearson's, covarying for age, was then carried out to determine if there was a relationship between SSRT and symptom severity. For all analyses, statistical significance was defined as $p < .01$. Effect sizes were calculated for all SST indices using partial eta squared.

RESULTS

There were significant group differences with regard to OCD symptomology (YBOCS), depression (HDRS), and general anxiety (HARS), with the OCD group showing higher levels of clinical symptoms as compared to the healthy controls. Forty-eight percent of OCD

participants had “sub-syndromal” symptoms, classified as a YBOCS score below 16. Analysis of covariance showed no between-group differences in mean direction errors, “go” reaction time, or percent inhibition on “stop” trials. There were significant differences in mean SSRT for both blocks ($F(2,61) = 6.00$; $p = .004$), with OCD participants having slower reaction times as compared to healthy controls. Effect sizes were medium to large (partial eta squared = 0.171). *Post hoc* analysis of blocks 1 and 2 independently indicated that the OCD group had higher SSRT across both blocks (Block 1: ($F(2,61)$) = 4.27; $p = .019$; Block 2: ($F(72,61)$) = 4.76; $p = .012$).

We also investigated the relation between SSRT and measures of symptom severity in the OCD group. Mean SSRT did not significantly correlate with measures of OCD current severity (YBOCS total score), depression (HDRS total score), or anxiety (HARS total score) in either block. Exploratory analyses showed that the OCD subgroup with YBOCS scores 16 or over ($n = 11$) had a mean SSRT of 196.83 (*SD* of 54.16), the OCD subgroup with YBOCS scores below 16 ($n = 10$) had a mean SSRT of 254.67 (*SD* of 53.24), and, as noted in Table 1, the HC group had a mean SSRT of 190.10 (*SD* of 40.13). Effect size for the above-threshold OCD group *versus* the HC group were small (partial eta squared = 0.004), and effect size for the below-threshold OCD group *versus* the HC group was large (partial eta squared = 0.274).

DISCUSSION

Previous studies have demonstrated impaired SSRT in OCD (Chamberlain et al., 2005, 2007; Menzies et al., 2007). Consistent with these findings, we found that OCD participants demonstrate impairments in SSRT in the absence of differences in mean reaction time or errors. In contrast to prior studies, we used participants with a lifetime diagnosis of OCD, and they may not have met diagnostic criteria for OCD (YBOCS > 16) at the time of the assessment. There was no relationship between SSRT and measures of depression, anxiety, or OCD severity. In fact, although the subgroups were small, and results should be interpreted with caution, the mean SSRT for the patients with YBOCS scores below what is considered threshold for OCD (YBOCS < 16) was surprisingly longer than those above threshold (YBOCS ≥ 16). As noted above, there was no clear relationship between OCD symptoms and SSRT. This may indicate that SSRT represents a trait, rather than a state effect of the disorder. However, future studies should examine the relationship with severity in a larger sample.

Given several limitations to this study (modest sample size, lack of independent replication, lack of information about how recently OCD has remitted), results should be interpreted with caution. Although the sample size was small, particularly in the OCD group, significant findings were demonstrated regardless. OCD participants also had multiple comorbidities, indicating that this deficit may not be specific to OCD. However, our sample was representative of a typical OCD sample, as OCD rarely exists alone. In addition, studies have failed to support significant impairment in SSRT in depression, the most common comorbidity in this sample (Lipszyc & Schachar, 2010).

Ninety percent of the OCD participants were also on medications, and 70% were on multiple psychiatric medications. The most common medications were SSRIs. This is likely related to the sampling frame, as most of the OCD participants were recruited from a hospital OCD clinic and were in psychiatric treatment. Studies have failed to support changes in SSRT with SRI medication use in controls (Chamberlain et al., 2006; Drueke et al., 2010). Alternatively, although the majority of patients were not on medications that have a large impact on noradrenaline, reuptake inhibition of this chemical may preferentially impact SSRT in rats (Bari, Eagle, Mar, Robinson, & Robbins, 2009) and humans (Chamberlain et al., 2006).

The inability to inhibit compulsive behaviors in the presence of an anxiety cue is a hallmark feature of OCD. The most effective treatment for OCD, exposure with response/ritual prevention (ERP), relies, at least in part, on this ability. Understanding the mechanisms behind response inhibition in OCD may enable us to use paradigms, such as the SST, as a predictor of outcome in behavior therapy or other therapies for OCD. Novel techniques may also be developed to improve patient's ability to inhibit rituals to improve response to ERP. Despite the limitations of this study, the results indicate that future research into response inhibition in OCD and related disorders, particularly with regard to relationship with clinical outcome, is warranted.

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Table 1.

Demographic and clinical characteristics of OCD and healthy control participants

	OCD Group (*N* = 21)	Healthy Controls (*N* = 40)
Variable	**Mean (SD)**	**Mean (SD)**
Age	42.95 (12.89)	35.13 (14.10)
Education	15.38 (2.09)	15.13 (2.33)
YBOCS	16.57 (7.70)	0.83 (1.91)
HDRS	15.19 (10.22)	1.55 (2.34)
HARS	11.43 (7.27)	1.58 (2.10)
Mean SSRT	224.37 (60.15)	190.10 (40.13)
Mean RT	631.62 (135.23)	615.45 (140.46)
Direction Errors	1.48 (2.57)	1.00(1.76)
Percent Inhibition	0.55 (0.07)	0.56 (0.06)

YBOCS = Yale-Brown Obsessive Compulsive Scale severity score; HDRS = Hamilton Depression Rating Scale; HARS = Hamilton Anxiety Rating Scale; SSRT = Stop Signal Reaction Time; RT = reaction time.